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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,399	12/03/2003	Liqun Luo	S03-250	7526

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/727,399	LUO ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *8-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/3/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is an original application filed December 3, 2003.

Claims 1-25 are pending.

Election/Restriction

Applicant's election of group I, and the species of fluorescent protein and transposase in the reply filed on August 19, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). With respect to the election of species, upon reconsideration it would not be an undue burden to examine the genus and each of the species recited in the claims. Accordingly, the species elections are withdrawn.

Claims 1-25 are pending. Claims 8-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 19, 2006. Claims 1-7, drawn to a transgenic mouse comprising a marker gene that has a recombinase site on two separate chromosomes and a recombinase are currently under examination.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically,

Claim 1(c) is vague and unclear in the recitation of "promotes" because it appears from the teaching in the specification it is the recombinase that causes the recombination between the target sites. It is unclear if recombination must occur even in the presences of all the structural elements of (a)-(c) to meet the metes and bounds of claim, or if they simply have to be present. Further, the embodiments following the limitations of (a)-(c) are unclear as to whether they are required method steps necessary for the claimed product, in particular since there is no absolute requirement that recombination occurs, only the possibility of promotion by the recombinase. Additionally, it is unclear if the sequences encoding the recombinase are part of the genome integrated into the chromosome of the transgenic mouse, or they can simply be provided by other means such as a viral vector. In the later case, would a transgenic mouse comprising (a) and (b) only meet the limitations of the claims when an exogenous vector was administered and fall outside the scope when the vector is depleted from the cell. Finally, the limitation of the "the second marker" in the steps following (a)-(c) are unclear since the previous portions of the claim

only refer to "a first marker". There is insufficient antecedent basis for this limitation in the claim.

Claims 6 and 7 are vague and unclear in the recitation of "restricted" because it is unclear if this a method step that is required by the product or simply a description of the physical and structural limitation of the product. Further, the claims appear indefinite since the time to which they are "restricted" appear to change what is encompassed by the claim, even though it is the same starting structural material. For example in claim 7, it is unclear if one is required to administer tamoxifen or doxycycline to meet the limitation of the claim to produce a product by process, or alternatively whether the a transgenic mouse having simply the structural elements is encompassed by the limitations of the claims.

Regarding claim 5, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Further, there is insufficient antecedent basis for the term "second marker" recited in claim 5 as it depends on claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Mao *et al.* (Blood 97(1):324-326, January 2001).

It is noted that a product is claimed, and the broadest reasonable interpretation would be a transgenic mouse comprising the elements of (a)-(c), that is a recombinase target site integrated at two homologous sites in the genome and the presence of a nucleic acid that encodes a recombinase that is present either on the chromosome or provided as an exogenous nucleic acid vector. Dependent claims indicate that the recombinase is Cre orFLP, and that the promoter regulates transcription in a cell-type specific way. The consequences of having these structural limitations would be inherent, therefore the limitations describing the segregation would be met by simply having the structural elements.

Mao *et al.* teach a transgenic mouse comprising in its genome loxP sites at homologous sites in the chromosome. Mao *et al.* teach that the expression of Cre by the lck promoter resulted in recombination and the presence of a detectable marker. To the extent that two different markers are required by the instant claims, Mao *et al.* demonstrate by Southern blot analysis that WT and excised sequences on either side of the LoxP sites are present.

Claims 1, 2, 5, 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawamoto *et al.* (FEBS 470:263-268, 2000).

The breadth of the claims are discussed above. Similar to Mao *et al.*, Kawamoto *et al.* teach a transgenic mouse that comprises in its genome LoxP sites positioned in a construct, wherein upon recombination detectable marker sequences on either side can be used to demonstrate that recombination has occurred. Kawamoto *et al.* teach to use the CAG promoter for cell specific expression of the recombinase Cre to affect the recombination of the transgenic mouse.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Liu *et al.* (Nature Genetics 30:66-72, January 2002) disclose the sue of FLP and Cre recombinase in mosue ES cells to study the segregation of mitotically recombined chromatids. In particular they demonstrate that this system is reproducible and a powerful tool to study mitotic recombination and to study the affect of genetic mosaics that are generated with said system (see for example page 70, second column discussion section).

Conclusion

No claim is allowed. Claims 3, 4 and 7 are free of the prior art of record because while the art teaches generally to use recombination sites and recombinases like Cre and FLP to affect recombination in the chromosome of a cell of a transgenic mouse, it fails to teach or provide motivation for using two markers encoding fluorescent proteins. More specifically, the breadth of the claims for a marker encompass using essentially any detectable sequence thus are anticipated by the structure of transgenic mice with conditional knockout constructs incorporated into their genome. While x- and z-segregation where known and studied in the art with respect to various endogenous markers, there is no teaching nor motivation to use exogenous markers, in particular sequences encoding two fluorescent proteins.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach